NOV 2 8 2000 K002262 ATTACHMENT III

SUMMARY OF SAFETY AND EFFECTIVENESS

Performance Characteristics

A. Comparison Testing

A total of five hundred and twenty-one sera were tested for the presence of HSV 1 & 2 IgM antibodies using the Diamedix Is-HSV1 & 2 IgM Test Kit and other marketed tests at two independent sites (site #1, California and site #2, New York) as well as at Diamedix Corp., Miami, FL (site #3). At site #3, testing was performed both manually and using the MAGO Plus Automated EIA Processor.

Site #1, a large commercial laboratory in California, not affiliated with the manufacturer, tested 132samples. These samples consisted of 100 fresh samples submitted to the laboratory for HSV IgM testing and 32 frozen samples which had previously tested positive for HSV IgM antibodies using EIA and/or IFA methods. Samples came from a wide variety of geographic locations and from patients with ages ranging from 1 day to 81 years old. For the fresh samples, 60 were from females and 39 from males. Forty of the females were between the ages of 18 and 45 but were not specifically identified as prenatal. The remaining sample was not identified as regards gender. The current testing protocol for HSV IgM testing at site #1 involves screening samples on separate HSV 1 and HSV 2 IgM EIA test kits. Samples with negative results are reported as such. Samples with positive or equivocal results in either EIA test are then tested using HSV 1 and HSV 2 IFA methods for purposes of confirmation. TABLE 1 summarizes the initial testing using the Diamedix Is-HSV 1 & 2 IgM Test Kit and the other EIA test kits.

Site #2, a commercial reference laboratory in New York, not affiliated with the manufacturer, tested 130 samples. These samples consisted of 65 fresh samples and 65 frozen samples submitted to the laboratory for HSV IgM testing. Samples were obtained from various geographic regions and from patients with ages rangingfrom 4 to 88 years old. Fifty samples were from males and seventy-four from females. The remainder were not identified as regards gender. Fifty of the females were 18-45 years old. TABLE 2 compares the results obtained for the Is-HSV IgM test kit and the HSV IgM EIA kits currently used by the laboratory.

TABLE 1

Is-HSV 1 & 2 IgM - Site #1

Other EIAs (Combined)	Positive	Negative	Equivocal
Positive	57	21	0
Negative	2	38	0
*Equivocal	0	0	14

Overall Agreement** 95/118 = 80.5% *95% CI** 73.4 to 82.7

TABLE 2

Is-HSV 1 & 2 IgM - Site #2

	Positive	Negative	Equivocal
Positive	27	2	3
Negative	14	77	3
*Equivocal	1	2	1

Overall Agreement** 104/120 = 86.7% *95% CI** 80.6 to 92.7

* Equivocal results excluded from calculations

** 95% Confidence Intervals (CI) calculated by the Exact Method

For Site #1, further testing of the discordant samples was performed by testing such samples using other methods. Of the 21 samples that were negative in the Is-HSV 1 & 2 IgM test but positive by the comparative EIA tests, all were negative in the confirmatory IFA test and 18 were negative in other EIA tests. Three were positive in the referee HSV 2 test. Of the 2 samples that were positive in the Is-HSV 1 & 2 IgM test and negative in the comparative tests, one was positive in the referee HSV 2 test.

For Site #2, further testing of the discordant samples was performed by testing such samples using other methods. Of the 2 samples that were negative in the Is-HSV 1 & 2 IgM test and positive in one of the two comparative tests, one was positive and one was negative in the referee (type 1 and 2) test. Of the 14 samples that were positive in the Is-HSV 1 & 2 IgM test and negative in the comparative tests, 12 were positive, one was equivocal and one was negative in the referee (type 1 and 2) test.

Site #3 (Diamedix Corp.) tested 259 samples (all frozen) by the manual method and 258 of these samples (one being QNS) by the MAGO Plus method. Two hundred of these samples were obtained from normal S. Florida blood donors and the remaining 59 sera from patients with positive serostatus. TABLES 3 and 4 compare the results obtained for the Is-HSV 1 & 2 IgM Test Kit and another marketed EIA test kit.

TABLE 3

Is-HSV 1 & 2 IgM - Site #3 : Manual

Other EIAs (combined)	Positive	Negative	Equivocal
Positive	74	17	7
Negative	10	138	4
*Equivocal	2	5	2

Overall Agreement** 212/239 = 88.7% *95% CI** 84.7 to 92.7

TABLE 4

Is-HSV 1 & 2 IgM- Site #3 : MAGO Plus

	Positive	Negative	Equivocal
Positive	74	12	12
Negative	13	123	15
*Equivocal	3	6	0

Overall Agreement** 197/222 = 88.7% *95% CI** 84.6 to 92.9

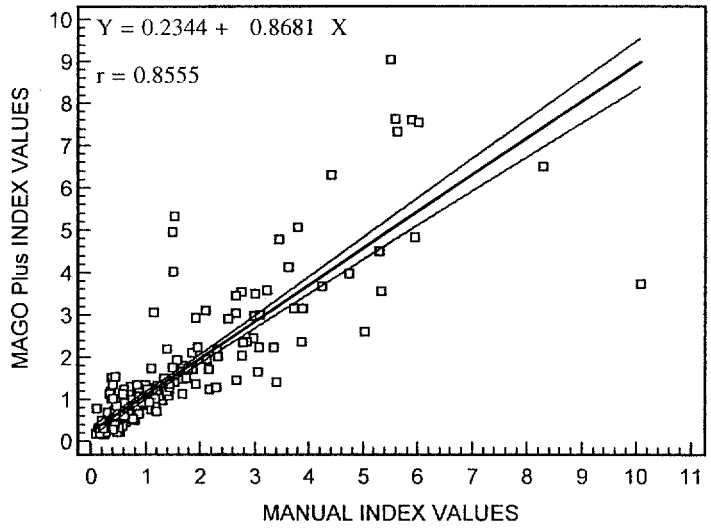
*Equivocal results excluded from calculations ** 95% Confidence Intervals (CI) calculated by the Exact Method (7)

For site #3 (manual testing), further testing of the discordant samples revealed that of the 10 samples positive in the Is-HSV 1 & 2 IgM and negative in the comparative methods, 5 were positive, 3 were equivocal and 2 were negative in the referee method. Of the 17 samples negative in the Is-HSV 1 & 2 IgM and positive in the comparative methods, 11 were negative, 5 were positive and one was equivocal in the referee method. For the MAGO Plus testing, of the 13 samples that were positive in the Is-method and negative in the comparative tests, 7 were negative, 4 were positive and 2 were equivocal in the referee test. Of the 12 samples that were negative in the Is-method and positive in the comparative methods, 8 were negative, 3 were positive and one was equivocal in the referee method.

B. Correlation of Manual and MAGO Plus Results

The Is-HSV 1 & 2 IgM Test Kit has been developed for automated as well as manual use. To demonstrate the equivalence of the manual and MAGO Plus procedures, the results of 258 serum samples tested above were compared. A scattergram and regression line of the results obtained with 95% confidence intervals is shown in FIGURE 1.

FIGURE 1 : Manual vs MAGO Plus Correlation



C. Cross-Reactivity/Interference Studies

The specificity of the Is-HSV 1 & 2 IgM Test Kit was assessed by testing a number of sera containing relatively high levels of IgM antibody to other viruses, including other herpesviruses. A total of 29 known IgM-positive samples were tested. In addition, the effects of potential interference from rheumatoid factor (RF), anti-nuclear antibody (ANA), viral-specific IgG and heterophile antibodies were assessed by testing an additional 33 sera. Results are summarized in TABLE 5 and show some cross-reactivity with Epstein Barr Virus (EBV), cytomegalovirus (CMV) and Toxoplasma.

In addition, some interference was noted in one highly positive RF sample and in some ANA positive samples. Note that several of these samples were also positive in a commercially available HSV IgM test. TABLE 6 shows the lack of interference in samples containing relatively high levels of IgG antibodies and low levels of IgM antibodies before and after removal of the IgG-class antibodies.

TABLE 5

Specificity	# of Positive in Is-HSV 1 & 2 IgM
EBV IgM	2/8
Lyme IgM	0/3
VZV IgM	0/4
Rubella IgM	0/4
CMV IgM	1/5
Toxoplasma IgM	2/5
Heterophile Ab	0/4
RF	1/8
ANA	5/10
HSV IgG	0/11

TABLE 6

	Before IgG removal		After IgG removal	
Sample #	IgG EU/ml	IgM Index	IgG EU/ml	IgM Index
1	65.6	1.313	0.0	1.121
2	87.1	1.592	0.0	1.530
3	89.0	1.962	0.0	2.119
4	57.1	1.438	0.0	1.255
5	61.0	1.412	0.0	1.197
6	56.5	1.414	0.0	1.212
7	91.1	1.990	0.0	1.815

(Pos > 20 EU/ml)

D. Verification of IgM Specificity

To confirm that the Is-HSV 1 & 2 IgM Test Kit specifically detects IgM-class antibodies, 13 samples with moderate to high levels of antibodies were selected for testing. These samples were treated with dithiothreitol (DTT) to destroy the IgM and were then retested in the Is-HSV 1 & 2 IgM Test Kit. The results in TABLE 7 show that these samples were rendered non-reactive following treatment with DTT confirming the specificity of the Is-HSV 1 & 2 IgM Test Kit for detecting IgM-class antibodies.

TABLE 7

	Untreated		Treated with DTT	
	Is-HSV 1 & 2 IgM		Is-HSV 1 & 2 IgM	
Sample #	Index	Interp	Index	Interp
1	3.279	POS	0.124	NEG
2	7.579	POS	0.482	NEG
3	4.804	POS	0.132	NEG
4	4.880	POS	0.381	NEG
5	3.252	POS	0.605	NEG
6	8.029	POS	1.054	EQUIV
7	3.986	POS	0.222	NEG
8	3.237	POS	0.173	NEG
9	4.421	POS	0.215	NEG
10	7.367	POS	0.511	NEG
11	7.182	POS	0.816	NEG
12	3.345	POS	0.633	NEG
13	5.975	POS	0.339	NEG

E. Precision

Six serum samples (two negative and four positive) as well as the kit Calibrator and controls were tested in triplicate in three separate runs for site #1 and #2 and in six separate runs for site #3. The precision studies were performed manually at the two independent testing sites (site #1 and site #2) and at site #3 (Diamedix Corp.) both manually and using the MAGO Plus Automated Processor. The results obtained are shown in Tables 8-11.

TABLE 8 : Site #1 - Intra-Assay and Interassay Precision

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
H1	0.205	0.023	11.22	0.236	0.037	15.68	0.212	0.012	5.66	0.218	0.027	12.39
H2	0.270	0.018	6.67	0.306	0.012	3.92	0.244	0.026	10.66	0.273	0.032	11.72
H3	1.377	0.088	6.39	1.406	0.020	1.42	1.429	0.084	5.88	1.404	0.066	4.70
H4	3.250	0.241	7.42	3.067	0.267	8.71	3.392	0.256	7.55	3.236	0.262	8.10
H5	4.232	0.004	0.09	3.818	0.187	4.90	4.362	0.232	5.32	4.137	0.288	6.96
H6	7.858	0.339	4.31	6.401	0.130	2.03	7.552	0.294	3.89	7.271	0.705	9.70
POS	1.819	0.020	1.10	1.815	0.239	13.17	1.719	0.244	14.19	1.784	0.178	9.98
NEG	0.264	0.017	6.44	0.329	0.058	17.63	0.266	0.067	25.19	0.287	0.055	19.16

TABLE 9 : Site #2 - Intra-Assay and Interassay Precision

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
H1	0.224	0.072	32.14	0.191	0.090	47.12	0.233	0.026	12.88	0.216	0.063	29.17
H2	0.286	0.111	38.81	0.182	0.012	6.59	0.319	0.024	8.46	0.262	0.084	32.06
H3	1.087	0.044	4.05	1.367	0.514	37.60	1.946	0.117	6.94	1.466	0.464	31.65
H4	2.294	0.184	8.02	2.968	0.080	2.70	3.076	0.275	10.31	2.780	0.412	14.82
H5	3.538	0.633	17.89	4.337	0.411	9.48	5.553	0.046	0.96	4.476	0.957	21.38
H6	5.967	0.078	1.31	6.599	1.139	17.26	9.606	0.714	8.57	7.391	1.825	24.69
CAL	1.149	0.400	34.81	0.854	0.150	17.56	1.364	0.203	17.17	1.122	0.329	29.32
POS	2.109	0.613	29.07	1.689	0.197	11.66	2.404	0.168	8.06	2.067	0.458	22.16
NEG	0.445	0.168	37.75	0.235	0.024	10.21	0.374	0.080	24.62	0.351	0.134	38.18

TABLE 10 : Site #3 - Intra-Assay and Interassay Precision (Manual)

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
A	0.191	0.035	18.32	0.193	0.070	36.27	0.161	0.017	10.56	0.181	0.046	25.41
B	0.316	0.049	15.51	0.268	0.018	6.72	0.235	0.019	8.09	0.273	0.045	16.48
C	1.388	0.058	4.18	1.283	0.089	6.94	1.202	0.058	4.83	1.291	0.102	7.90
D	3.424	0.085	2.48	2.646	0.280	10.58	2.398	0.107	4.46	2.823	0.481	17.04
E	5.772	0.490	8.49	4.644	0.459	9.88	4.495	0.564	12.55	4.970	0.755	15.19
F	8.538	0.825	9.66	7.668	0.469	6.12	7.339	0.750	10.22	7.848	0.837	10.67
c/o CAL	1.019	0.099	9.72	0.900	0.068	7.56	0.894	0.055	6.15	0.938	0.093	9.91
POS	1.474	0.144	9.77	1.233	0.182	14.76	1.334	0.162	12.14	1.347	0.184	13.66
NEG	0.351	0.054	15.38	0.291	0.054	18.56	0.346	0.105	30.35	0.329	0.076	23.10

TABLE 11 : Site #3 - Intra-assay and Interassay Precision (MAGO Plus)

SERUM	INTRA-ASSAY DAY 1			INTRA-ASSAY DAY 2			INTRA-ASSAY DAY 3			INTERASSAY		
	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%	MEAN INDEX	SD	CV%
A	0.22	0.059	26.82	0.23	0.046	20.00	0.25	0.037	14.80	0.23	0.05	21.74
B	0.35	0.053	15.14	0.36	0.025	6.94	0.38	0.053	13.95	0.36	0.05	13.89
C	1.39	0.121	8.71	1.42	0.120	8.45	1.47	0.136	9.25	1.43	0.12	8.39
D	2.69	0.478	17.77	2.54	0.263	10.35	2.54	0.293	11.54	2.59	0.34	13.13
E	6.05	0.377	6.23	5.30	0.322	6.08	5.35	0.384	7.18	5.57	0.49	8.80
F	8.33	0.509	6.11	7.62	0.681	8.94	7.86	0.537	6.83	7.94	0.62	7.81
c/o CAL	0.96	0.113	11.77	1.00	0.110	11.00	1.25	0.091	7.28	1.07	0.16	14.95
POS	1.42	0.289	20.35	1.22	0.283	23.20	1.32	0.096	7.27	1.32	0.24	18.18
NEG	0.37	0.143	38.65	0.40	0.060	15.00	0.44	0.089	20.23	0.40	0.10	25.00

Expected Values

The prevalence of HSV IgM antibodies can vary depending on a number of factors such as age, gender, geographical location, socio-economic status, race, sexual behavior, testing method used, specimen collection and handling procedures and clinical and epidemiological history of individual patients.

In the present study two hundred sera from South Florida blood donors were evaluated in the Is-HSV 1 & 2 IgM Test Kit. These sera were derived from 102 female donors and 98 male donors. Of these samples one hundred and fifty-eight (79%) were negative, thirty-two (16%) were positive and ten (5%) were equivocal. TABLE 12 shows the age and prevalence profile for this population. FIGURE 2 presents a histogram showing the distribution of Index values obtained. FIGURE 3 shows the distribution of values in the 59 positive samples tested by Diamedix. In addition to these samples, 77 sera from pregnant females were tested. For this group, 55 (71.4%) were negative, 13 (16.9%) were positive and 9 (11.7%) were equivocal for HSV IgM antibodies using the Is-HSV 1 & 2 IgM Test kit.

TABLE 12: Age Distribution and Prevalence of anti-HSV 1 & IgM in a Normal S. Florida Population

	Number of Donors	% Seronegative	% Seropositive	% Equivocal
Total Number	200	79.0% (158)	16.0% (32)	5.0% (10)
Geographic Location: S. Fla	200			
Age: 10-19	18	77.8% (14)	22.2% (4)	0.0% (0)
20-29	47	70.2% (33)	23.4% (11)	6.4% (3)
30-39	74	81.1% (60)	13.5% (10)	5.4% (4)
40-49	40	80.0% (32)	12.5% (5)	7.5% (3)
50-59	11	100.0% (11)	0.0% (0)	0.0% (0)
60-69	9	77.8% (7)	22.2% (2)	0.0% (0)
>70	1	100.0% (1)	0.0% (0)	0.0% (0)
Gender				
Male	98	87.7% (86)	9.2% (9)	3.1% (3)
Females	102	70.6% (72)	22.5% (23)	6.9% (7)

FIGURE 2

Distribution of Is-HSV 1 & 2 IgM Results in a Normal Population

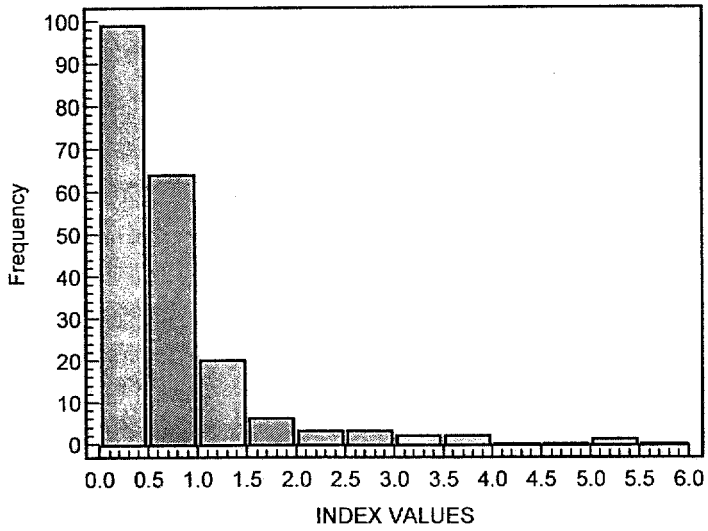
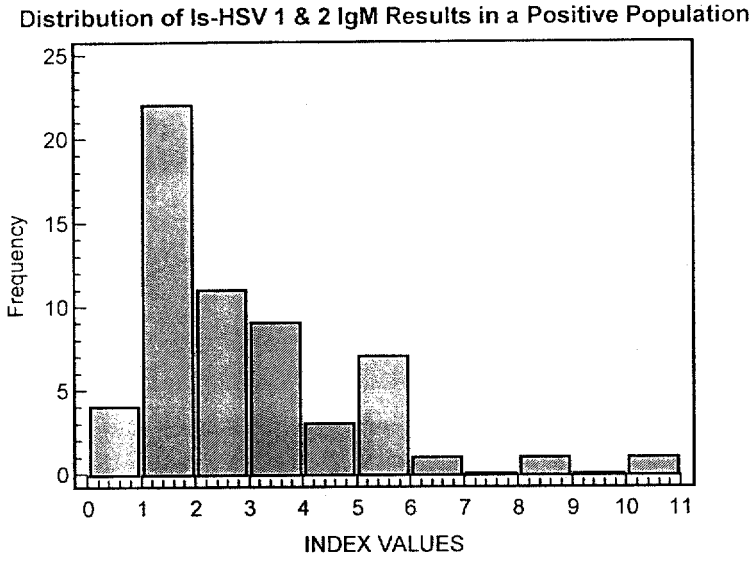


FIGURE 3


Distribution of Is-HSV 1 & 2 IgM Results in a Positive Population
Frequency
25
20
15
10
5
0
0 1 2 3 4 5 6 7 8 9 10 11
INDEX VALUES

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 2 8 2000

Lynne Stirling, Ph.D.
Diamedix Corporation
2140 N. Miami Avenue
Miami, Florida 33127

Re: K002262
Trade Name: Is-HSV 1 & 2 IgM Test System
Regulatory Class: III
Product Code: LGC
Dated: September 21, 2000
Received: September 22, 2000

Dear Dr. Stirling:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

ATTACHMENT IV

Appendix G. Rev. Indications for Use Statement

INDICATIONS FOR USE STATEMENT

510(K) NUMBER : K002262

DEVICE NAME : Is-HSV 1 & 2 IgM Test System

Indications for Use : The Diamedix Is-HSV 1 & 2 IgM is an indirect Enzyme Immunoassay (EIA) for the qualitative determination of IgM antibodies to herpes simplex virus (HSV) type 1 and/or type 2 in human serum. This test can aid in the serologic evaluation of primary or reactivated infection with HSV. These reagents can be used either manually or in conjunction with the MAGO® Plus Automated EIA Processor. The performance of this assay has not been established for use in neonates, infants, or on cord blood, and immunocompromised patients.

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K002262

PRESCRIPTION USE X